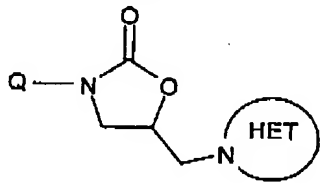
Application No. 10/550,038
Amendment Dated 05/18/2006
Reply to Office Action of 04/13/2006

**In the Claims**

The listing of claims will replace all prior versions and listings of claims in the application.

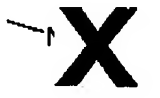
**Listings of claim**

1. (Currently Amended) A compound of the formula (I), or a pharmaceutically-acceptable salt, or an in-vivo-hydrolysable ester thereof,



(I)

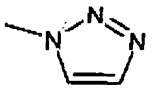
wherein -N-HET is ~~selected from the structures (Ia) to (If) below~~ :-



(Ia)

(Ib)

(Ic)

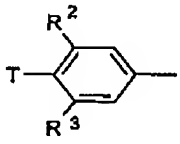


(Id)

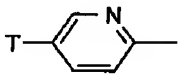
(Ie)

(If)

Q is ~~selected from Q1 to Q6~~



Q1 or



Q2

Q3

Q4

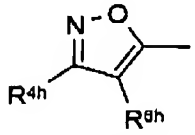
Q5

Q6

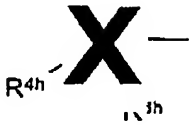
$R_2$ and $R_3$ are independently selected from H, F, Cl, $CF_3$, OMe, SMe, Me and Et;

~~$B_4$ is O or S;~~

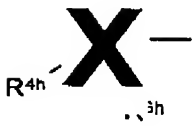
T is selected from the groups in (TAa1) to (TAa12):



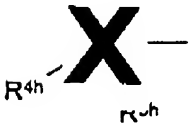
(TAa1)



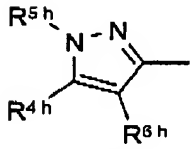
(TAa2)



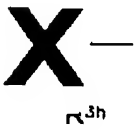
(TAa3)



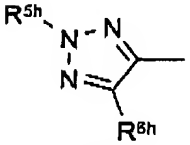
(TAa4)



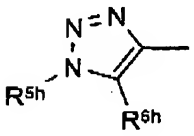
(TAa5)



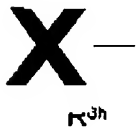
(TAa6)



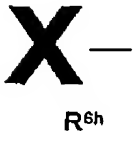
(TAa7)



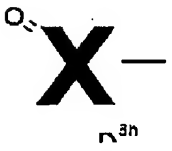
(TAa8)



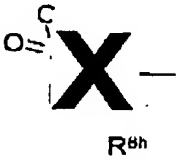
(TAa9)



(TAa10)



(TAa11)



(TAa12)

wherein :

$R^{6h}$ is hydrogen or (1-4C)alkyl;

$R^{4h}$ and $R^{5h}$ are independently selected from hydrogen, cyano, hydroxy(1-4C)alkyl, cyano(1-4C)alkyl, phosphoryl(1-4C)alkyl, benzyl (optionally substituted on the phenyl ring by one substituent selected from halo, methyl and methoxy), (1-4C)alkyl, (1-4C)alkyl substituted with ORc (wherein Rc is $R^{13}CO$ and $R^{13}$ is selected from Rc2b), (1-4C)alkanoyl and (1-4C)alkoxycarbonyl,

~~$R^{6h}$ is selected from hydrogen, (1-4C)alkyl, (1-4C)alkoxycarbonyl, (1-4C)alkanoyl, carbamoyl and cyano;~~

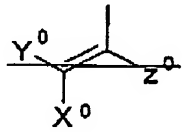
~~$R^{4h}$ and $R^{5h}$ are independently selected from hydrogen, halo, trifluoromethyl, cyano, nitro, (1-4C)alkoxy, (1-4C)alkylS(O)$_q$ (q is 0, 1 or 2), (1-4C)alkanoyl, (1-4C)alkoxycarbonyl, benzyloxy-(1-4C)alkyl, (2-4C)alkanoylamino, CONRcRv and NRcRv wherein any (1-4C)alkyl group contained in the preceding values for $R^{4h}$ and $R^{5h}$ is optionally substituted by~~

up to three substituents independently selected from hydroxy (not on C1 of an alkoxy group, and excluding geminal disubstitution), oxo, trifluoromethyl, cyano, nitro, (1-4C)alkoxy, (2-4C)alkanoyloxy, hydroxyimino, (1-4C)alkoxyimino, (1-4C)alkylS(O)$_q$- (q is 0, 1 or 2), (1-4C)alkylSO$_2$-NRv-, (1-4C)alkoxycarbonyl, -CONRcRv, and -NRcRv (not on C1 of an alkoxy group, and excluding geminal disubstitution); wherein Rv is hydrogen or (1-4C)alkyl and Rc is as hereinafter defined;

R$^{4h}$ and R$^{6h}$ may further be independently selected from (1-4C)alkyl [optionally substituted by one, two or three substituents independently selected from hydroxy (excluding geminal disubstitution), oxo, trifluoromethyl, cyano, nitro, (1-4C)alkoxy, (2-4C)alkanoyloxy, phosphoryl [-O-P(O)(OH)$_2$, and mono- and di-(1-4C)alkoxy derivatives thereof], phosphiryl [-O-P(OH)$_2$ and mono- and di-(1-4C)alkoxy derivatives thereof], hydroxyimino, (1-4C)alkoxyimino, (1-4C)alkylS(O)$_q$- (q is 0, 1 or 2), (1-4C)alkylSO$_2$-NRv-, (1-4C)alkoxycarbonyl, -CONRcRv, -NRcRv (excluding geminal disubstitution), ORc, and phenyl (optionally substituted by one, two or three substituents independently selected from (1-4C)alkyl, (1-4C)alkoxy and halo)]; wherein Rv is hydrogen or (1-4C)alkyl and Rc is as hereinafter defined; and wherein any (1-4C)alkyl group contained in the immediately preceding optional substituents (when R$^{4h}$ and R$^{6h}$ are independently (1-4C)alkyl) is itself optionally substituted by up to three substituents independently selected from hydroxy (not on C1 of an alkoxy group, and excluding geminal disubstitution), oxo, trifluoromethyl, cyano, nitro, (1-4C)alkoxy, (2-4C)alkanoyloxy, hydroxyimino, (1-4C)alkoxyimino, (1-4C)alkylS(O)$_q$- (q is 0, 1 or 2), (1-4C)alkylSO$_2$-NRv-, (1-4C)alkoxycarbonyl, -CONRcRv, and -NRcRv (not on C1 of an alkoxy group, and excluding geminal disubstitution); wherein Rv is hydrogen or (1-4C)alkyl and Rc is as hereinafter defined;

or R$^{4h}$ is selected from one of the groups in (TAaa) to (TAab) below, or (where appropriate) one of R$^{4h}$ and R$^{6h}$ is selected from the above list of R$^{4h}$ and R$^{6h}$ values, and the other is selected from one of the groups in (TAaa) to (TAab) below :-

*(TAaa)* a group of the formula (TAaa1)




(TAaa1)

wherein Z$^0$ is hydrogen or (1-4C)alkyl;

X$^0$ and Y$^0$ are independently selected from hydrogen, (1-4C)alkyl, (1-4C)alkoxycarbonyl, halo, cyano, nitro, (1-4C)alkylS(O)$_q$- (q is 0, 1 or 2), RvRwNSO$_2$-, trifluoromethyl,

~~pentafluoroethyl, (1-4C)alkanoyl and -CONRvRw [wherein Rv is hydrogen or (1-4C)alkyl; Rw is hydrogen or (1-4C)alkyl];~~

~~*(TAab)* an acetylene of the formula -C≡H or -C≡(1-4C)alkyl;~~

~~wherein Rc is selected from groups (Rc1) to (Rc2) :-~~

~~*(Rc1)* (1-6C)alkyl [optionally substituted by one or more (1-4C)alkanoyl groups (including geminal disubstitution) and/or optionally monosubstituted by cyano, (1-4C)alkoxy, trifluoromethyl, (1-4C)alkoxycarbonyl, phenyl (optionally substituted as for AR1 defined hereinafter), (1-4C)alkylS(O)$_q$ (q is 0, 1 or 2); or, on any but the first carbon atom of the (1-6C)alkyl chain, optionally substituted by one or more groups (including geminal disubstitution) each independently selected from hydroxy and fluoro, and/or optionally monosubstituted by oxo, -NRvRw [wherein Rv is hydrogen or (1-4C)alkyl; Rw is hydrogen or (1-4C)alkyl], (1-6C)alkanoylamino, (1-4C)alkoxycarbonylamino, N-(1-4C)alkyl-N-(1-6C)alkanoylamino, (1-4C)alkylS(O)$_p$NH- or (1-4C)alkylS(O)$_p$-((1-4C)alkyl)N- (p is 1 or 2)];~~

~~*(Rc2)* -$R^{13}$CO-, -$R^{13}SO_2$- or -$R^{13}$CS-~~

~~wherein $R^{13}$ is selected from (Rc2a) to (Rc2d) :-~~

~~*(Rc2a)* hydrogen, (1-4C)alkoxycarbonyl, trifluoromethyl and -NRvRw [wherein Rv is hydrogen or (1-4C)alkyl; Rw is hydrogen or (1-4C)alkyl];~~

***(Rc2b)*** (1-10C)alkyl

{optionally substituted by one or more groups (including geminal disubstitution) each independently selected from hydroxy, (1-10C)alkoxy, (1-4C)alkoxy-(1-4C)alkoxy, (1-4C)alkoxy-(1-4C)alkoxy-(1-4C)alkoxy, (1-4C)alkanoyl, carboxy, phosphoryl [-O-P(O)(OH)$_2$, and mono- and di-(1-4C)alkoxy derivatives thereof], phosphiryl [-O-P(OH)$_2$ and mono- and di-(1-4C)alkoxy derivatives thereof], and amino; and/or optionally substituted by one group selected from phosphonate [phosphono, -P(O)(OH)$_2$, and mono- and di-(1-4C)alkoxy derivatives thereof], phosphinate [-P(OH)$_2$ and mono- and di-(1-4C)alkoxy derivatives thereof], cyano, halo, trifluoromethyl, (1-4C)alkoxycarbonyl, (1-4C)alkoxy-(1-4C)alkoxycarbonyl, (1-4C)alkoxy-(1-4C)alkoxy-(1-4C)alkoxycarbonyl, (1-4C)alkylamino, di((1-4C)alkyl)amino, (1-6C)alkanoylamino, (1-4C)alkoxycarbonylamino, N-(1-4C)alkyl-N-(1-6C)alkanoylamino, (1-4C)alkylaminocarbonyl, di((1-4C)alkyl)aminocarbonyl, (1-4C)alkylS(O)$_p$NH-, (1-4C)alkylS(O)$_p$-((1-4C)alkyl)N-, fluoro(1-4C)alkylS(O)$_p$NH-, fluoro(1-4C)alkylS(O)$_p$((1-4C)alkyl)N-, (1-4C)alkylS(O)$_q$- [the (1-4C)alkyl group of (1-4C)alkylS(O)$_q$- being optionally substituted by one substituent selected from hydroxy, (1-4C)alkoxy, (1-4C)alkanoyl, phosphoryl [-O-P(O)(OH)$_2$, and mono- and di-(1-4C)alkoxy derivatives thereof], phosphiryl [-O-P(OH)$_2$ and mono- and di-(1-4C)alkoxy derivatives thereof], amino, cyano, halo, trifluoromethyl, (1-4C)alkoxycarbonyl, (1-4C)alkoxy-(1-4C)alkoxycarbonyl, (1-4C)alkoxy-(1-4C)alkoxy-(1-4C)alkoxycarbonyl, carboxy, (1-4C)alkylamino, di((1-

4C)alkyl)amino, (1-6C)alkanoylamino, (1-4C)alkoxycarbonylamino, N-(1-4C)alkyl-N-(1-6C)alkanoylamino, (1-4C)alkylaminocarbonyl, di((1-4C)alkyl)aminocarbonyl, (1-4C)alkylS(O)$_p$NH-, (1-4C)alkylS(O)$_p$-((1-4C)alkyl)N-, and (1-4C)alkylS(O)$_q$-;

~~*(Rc2c)* $R^{14}C(O)O(1\text{-}6C)$alkyl wherein $R^{14}$ is AR1, AR2, (1-4C)alkylamino (the (1-4C)alkyl group being optionally substituted by (1-4C)alkoxycarbonyl or by carboxy), benzyloxy (1-4C)alkyl or (1-10C)alkyl (optionally substituted as defined for (Rc2b));~~

~~*(Rc2d)* $R^{15}O$- wherein $R^{15}$ is benzyl, (1-6C)alkyl (optionally substituted as defined for (Rc2c)) or AR2b;~~

~~wherein~~

~~AR1 is an optionally substituted phenyl or optionally substituted naphthyl;~~

~~AR2 is an optionally substituted 5- or 6-membered, fully unsaturated monocyclic heteroaryl ring containing up to four heteroatoms independently selected from O, N and S (but not containing any O-O, O-S or S-S bonds), and linked via a ring carbon atom, or a ring nitrogen atom if the ring is not thereby quaternised;~~

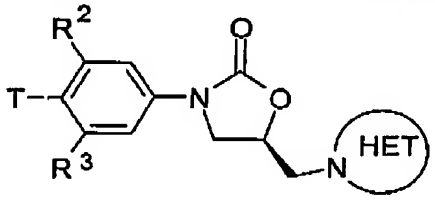
~~AR2a is a partially hydrogenated version of AR2, linked via a ring carbon atom or linked via a ring nitrogen atom if the ring is not thereby quaternised;~~

~~AR2b is a fully hydrogenated version of AR2, linked via a ring carbon atom or linked via a ring nitrogen atom.~~

2. (Previously Amended) A The compound of claim 1, wherein Q is Q1.

4. (Previously Amended) The compound of claim 1, wherein $R^2$ and $R^3$ are independently hydrogen or fluoro.

6. (Currently Amended) The compound of claim 1, which is a compound of formula (IB)




(IB)

wherein -N-HET is 1,2,3-triazol-1-yl or tetrazol-2-yl;

$R^2$ and $R^3$ are independently hydrogen or fluoro;

~~T is selected from TAa1, TAa5, TAa7 and TAa8;~~

$R^{6h}$ is hydrogen or (1-4C)alkyl;

$R^{4h}$ and $R^{5h}$ are independently selected from hydrogen, cyano, hydroxy(1-4C)alkyl, cyano(1-4C)alkyl, phosphoryl(1-4C)alkyl, benzyl (optionally substituted on the phenyl ring by one

substituent selected from halo, methyl and methoxy), (1-4C)alkyl, (1-4C)alkyl substituted with ORc (wherein Rc is $R^{13}CO$ and $R^{13}$ is selected from Rc2b), (1-4C)alkanoyl and (1-4C)alkoxycarbonyl.

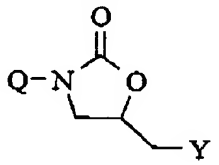
8. (Previously Amended) A method for producing an antibacterial effect in a warm blooded animal which comprises administering to said animal an effective amount of a compound of claim 1.

11. (Currently Amended) A pharmaceutical composition which comprises a compound of claim 1, and a pharmaceutically-acceptable diluent or carrier.

12. (Original) A process for the preparation of a compound of formula (I) as claimed in claim 1 or pharmaceutically acceptable salts or in-vivo hydrolysable esters or pro-drugs thereof, which process comprises one of processes **(a)** to **(g)**:

**(a)** by modifying a substituent in, or introducing a new substituent into, the substituent group Q of another compound of formula (I) ; or

**(b)** by reaction of a compound of formula (II) :



(II)

wherein Y is a displaceable group with a compound of the formula (III) :

-N-HET

(III)

wherein –N-HET (of formula (Ie) to (If) optionally protected) is HN-HET (free-base form) or N-HET anion formed from the free base form; or

**(c)** by reaction of a compound of the formula (IV) :

Q-Z

(IV)

wherein Z is an isocyanate, amine or urethane group with an epoxide of the formula (V) wherein the epoxide group serves as a leaving group at the terminal C-atom and as a protected hydroxy group at the internal C-atom; or with a related compound of formula (VI) where

the hydroxy group at the internal C-atom is protected and where the leaving group Y at the terminal C-atom is a leaving group;

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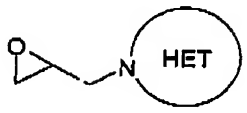
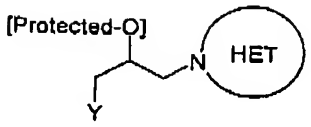


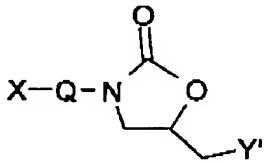

(V)




(VI)

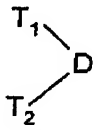
or

**(d) (i)** by coupling, using catalysis by transition metals, of a compound of formula (VII) :




(VII)

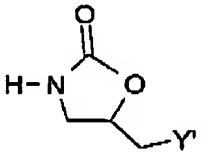
wherein Y' is a group –N-HET as hereinbefore defined, X is a replaceable substituent; with a compound of the formula (VIII), or an analogue thereof, which is suitable to give a T substituent as defined by (TAa1–TAa12) in which the link is via an $sp^2$ carbon atom (D = CH=C-Lg where Lg is a leaving group; or as in the case of reactions carried out under Heck reaction conditions Lg may also be hydrogen)




(VIII)

where $T_1$ and $T_2$ may be the same or different and comprise a precursor to a ring of type T as hereinbefore defined, or $T_1$ and $T_2$ may together with D form a ring of type T as hereinbefore defined;

**(d) (ii)** by coupling, using catalysis by transition metals, of a compound of formula (VIIA):




(VIIA)

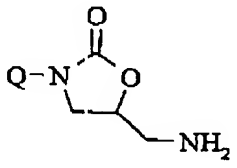
wherein Y' is a group HET as hereinbefore defined, with a compound

[Aryl]-X

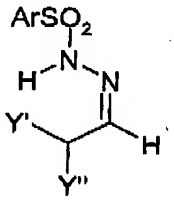
where X is a replaceable substituent;

**(e)** Where N-HET is 1,2,3-triazole by cycloaddition via the azide (wherein Y in (II) is azide), with acetylene or masked acetylene;

(f) Where N-HET is 1,2,3-triazole by synthesis with a compound of formula (IX), namely the arenesulfonylhydrazone of acetaldehyde, by reaction of a compound of formula (II) where Y = $NH_2$ (primary amine);

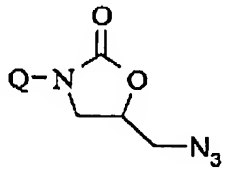


(II : Y = NH2)



(IX)

(g) Where N-HET is 1,2,3-triazole by cycloaddition via the azide (wherein Y in (II) is azide) with acetylene using Cu(I) catalysis in to give the N-1,2,3-triazole;



(II : Y = $N_3$)

and thereafter if necessary :

i) removing any protecting groups;

ii) forming a pro-drug (for example an in-vivo hydrolysable ester); and/or

iii) forming a pharmaceutically-acceptable salt.

13. A compound which is

(5*R*)-3-[3-Fluoro-4-(3-methylisoxazol-5-yl)phenyl]-5-(1*H*-1,2,3-triazol-1-ylmethyl)-1,3-oxazolidin-2-one;

Ethyl 5-{2-fluoro-4-[(5*R*)-2-oxo-5-(1*H*-1,2,3-triazol-1-ylmethyl)-1,3-oxazolidin-3-yl]phenyl}isoxazole-3-carboxylate;

(5*R*)-3-{3-Fluoro-4-[3-(hydroxymethyl)isoxazol-5-yl]phenyl}-5-(1*H*-1,2,3-triazol-1-ylmethyl)-1,3-oxazolidin-2-one;

(5-{2-Fluoro-4-[(5*R*)-2-oxo-5-(1*H*-1,2,3-triazol-1-ylmethyl)-1,3-oxazolidin-3-yl]phenyl}isoxazol-3-yl)methyl dihydrogen phosphate;

1-Methyl-3-{4-[(5*R*)-2-oxo-5-(1*H*-1,2,3-triazol-1-ylmethyl)-1,3-oxazolidin-3-yl]phenyl}-1*H*-pyrazole-5-carbonitrile;

1-Methyl-3-{4-[(5*R*)-2-oxo-5-(1*H*-1,2,3-triazol-1-ylmethyl)-1,3-oxazolidin-3-yl]phenyl}-1*H*-pyrazole-5-carbaldehyde;

(5*R*)-3-[3-Fluoro-4-(1*H*-1,2,3-triazol-4-yl)phenyl]-5-(1*H*-1,2,3-triazol-1-ylmethyl)-1,3-

oxazolidin-2-one;

(5*R*)-3-[3-Fluoro-4-(1-methyl-1*H*-1,2,3-triazol-4-yl)phenyl]-5-(1*H*-1,2,3-triazol-1-ylmethyl)-1,3-oxazolidin-2-one;

(5*R*)-3-[3-Fluoro-4-(2-methyl-2*H*-1,2,3-triazol-4-yl)phenyl]-5-(1*H*-1,2,3-triazol-1-ylmethyl)-1,3-oxazolidin-2-one;

(4-{2-Fluoro-4-[(5*R*)-2-oxo-5-(1*H*-1,2,3-triazol-1-ylmethyl)-1,3-oxazolidin-3-yl]phenyl}-1*H*-1,2,3-triazol-1-yl)acetonitrile; or

(4-{2-Fluoro-4-[(5*R*)-2-oxo-5-(1*H*-1,2,3-triazol-1-ylmethyl)-1,3-oxazolidin-3-yl]phenyl}-2*H*-1,2,3-triazol-2-yl)acetonitrile.